

1/59

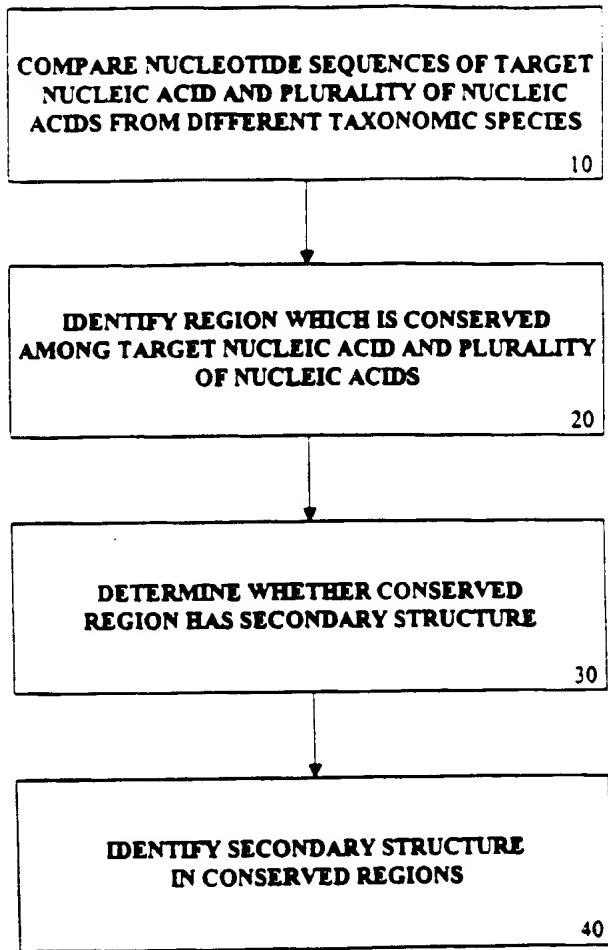


FIGURE 1

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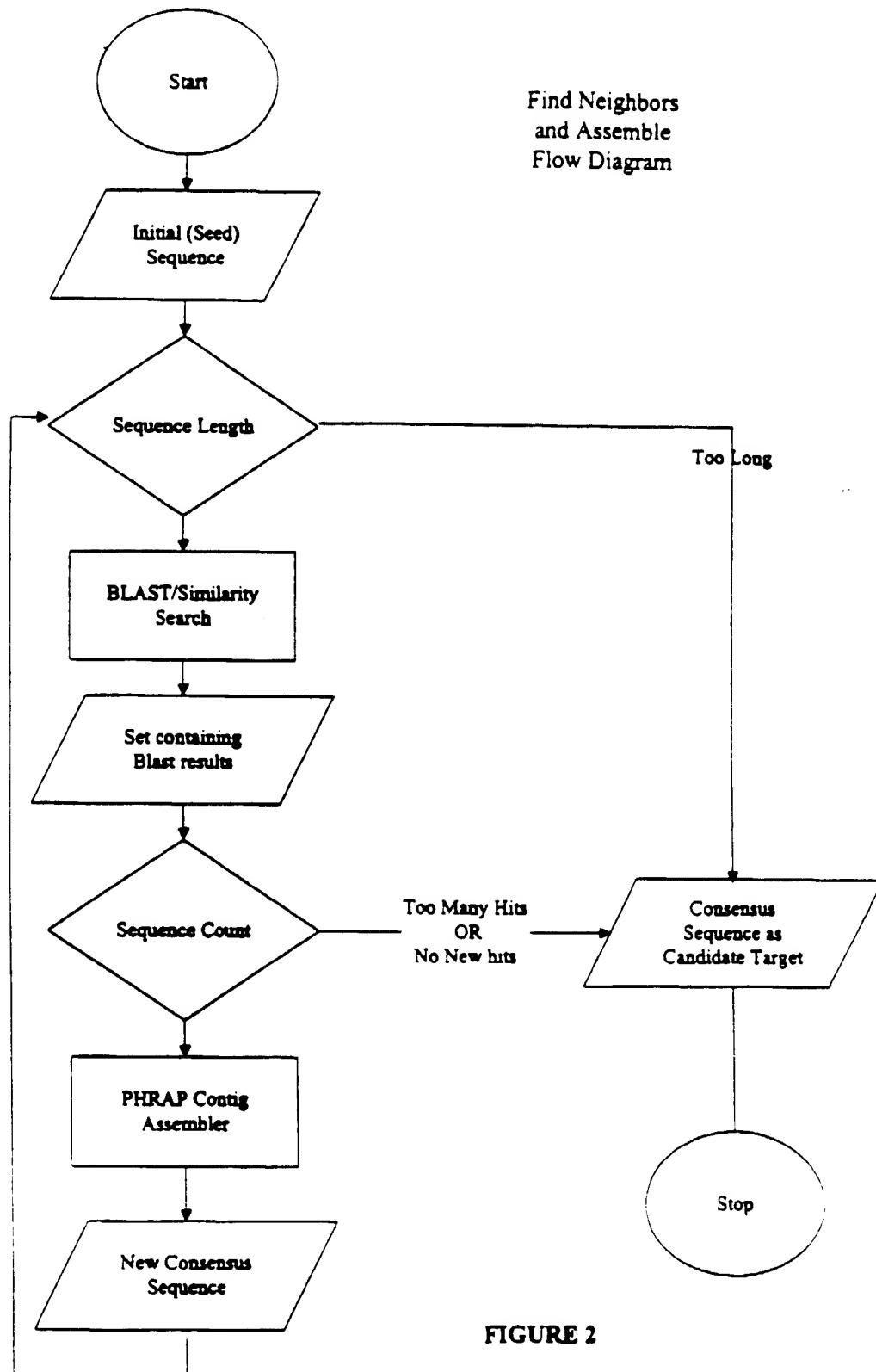


FIGURE 2

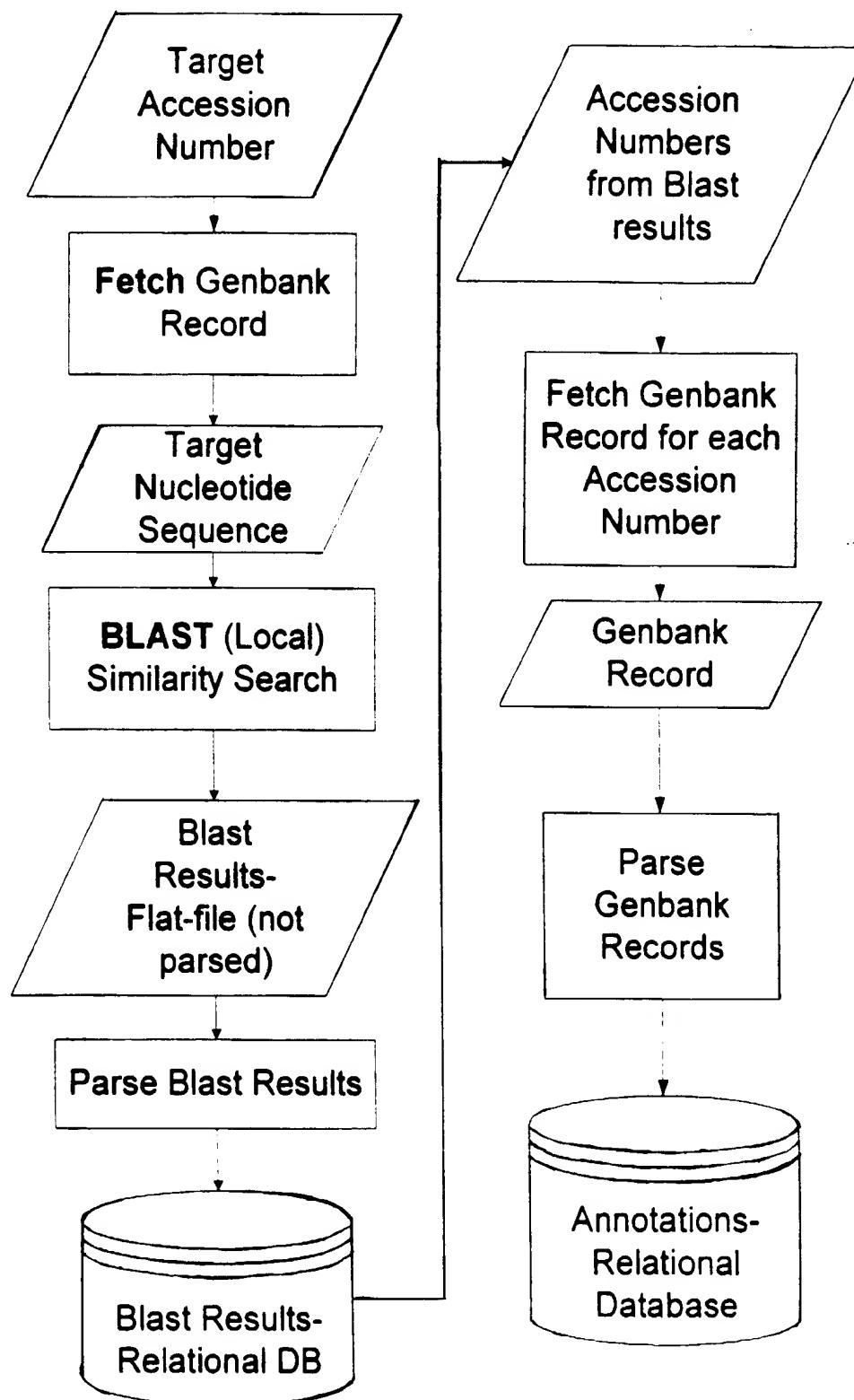


Figure 3

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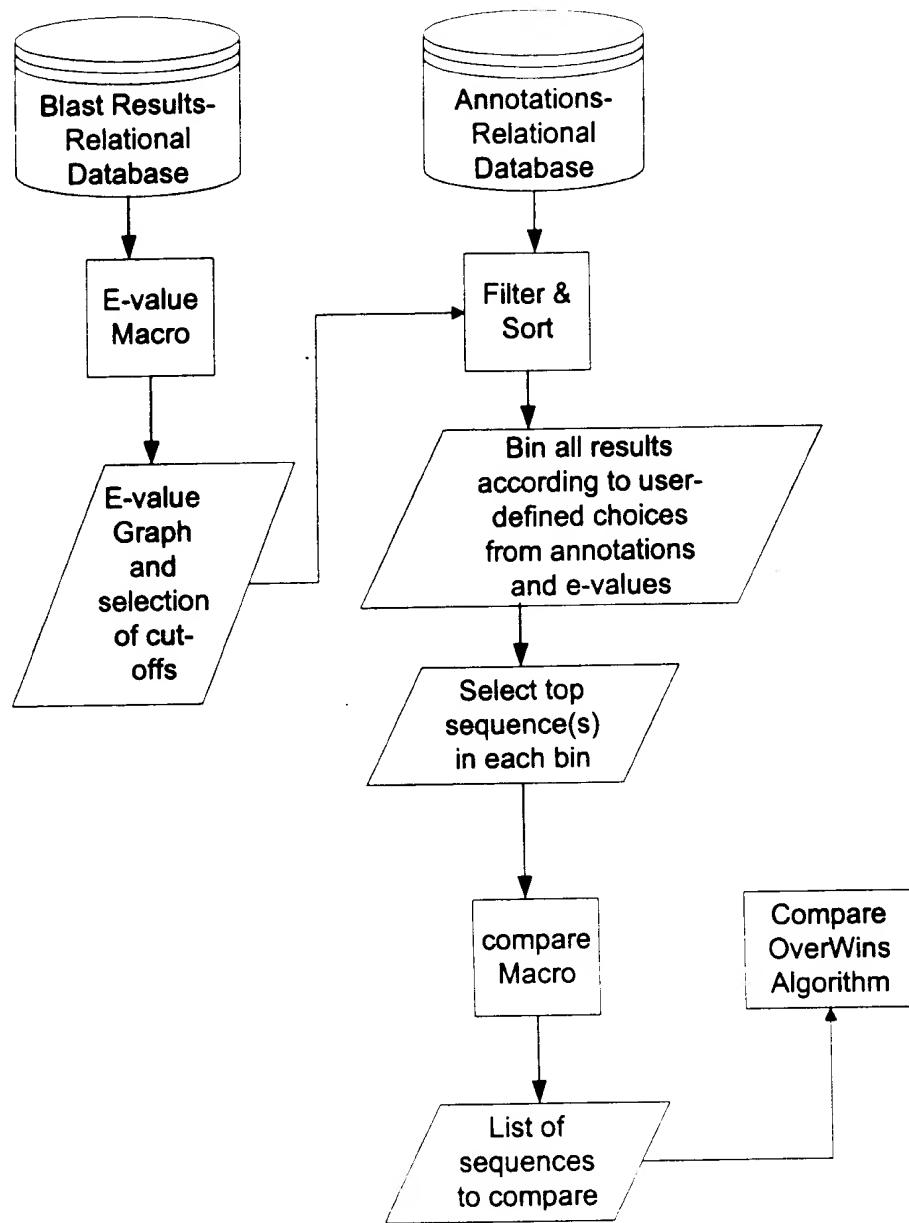


FIGURE 4

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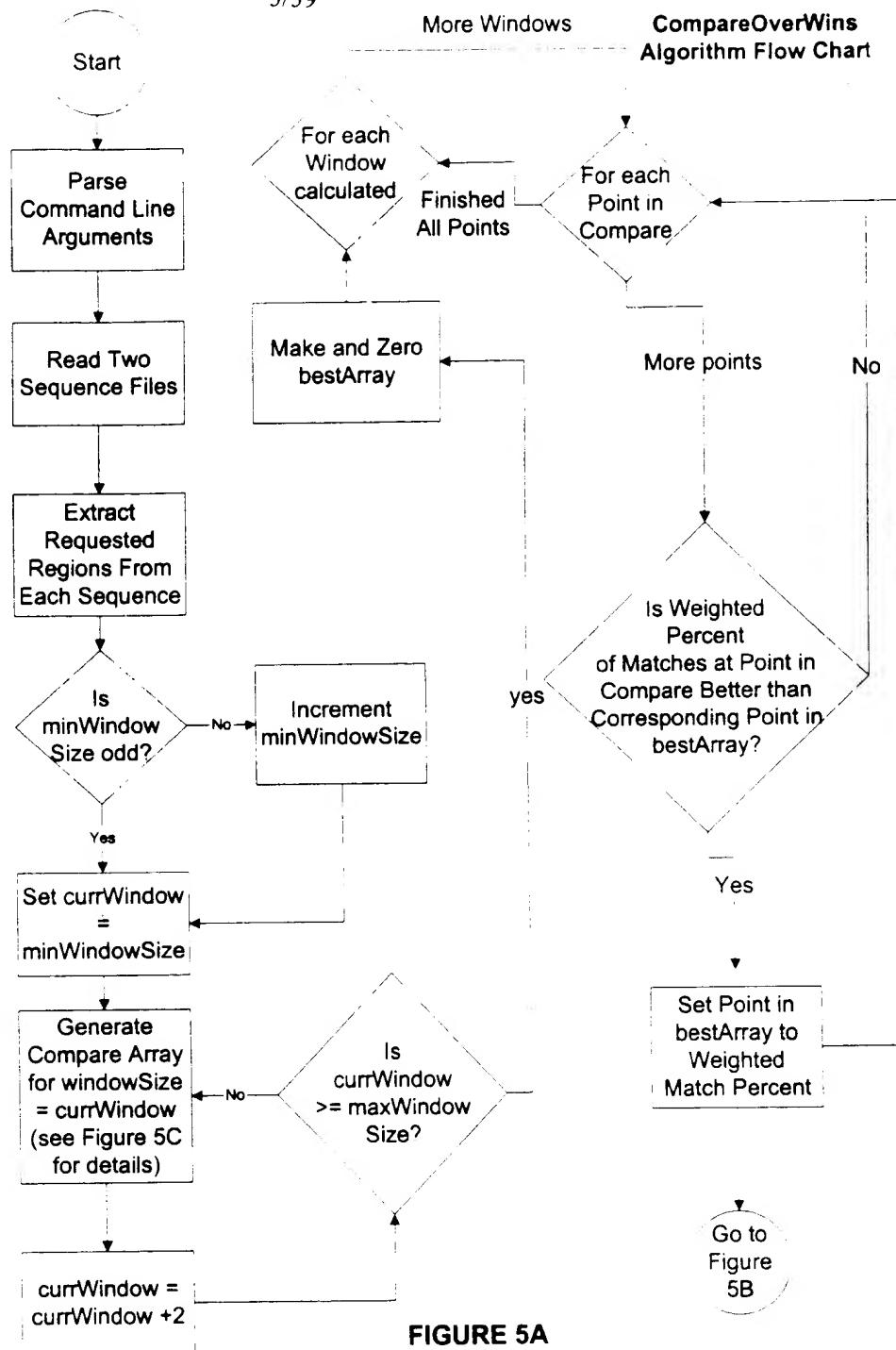


FIGURE 5A

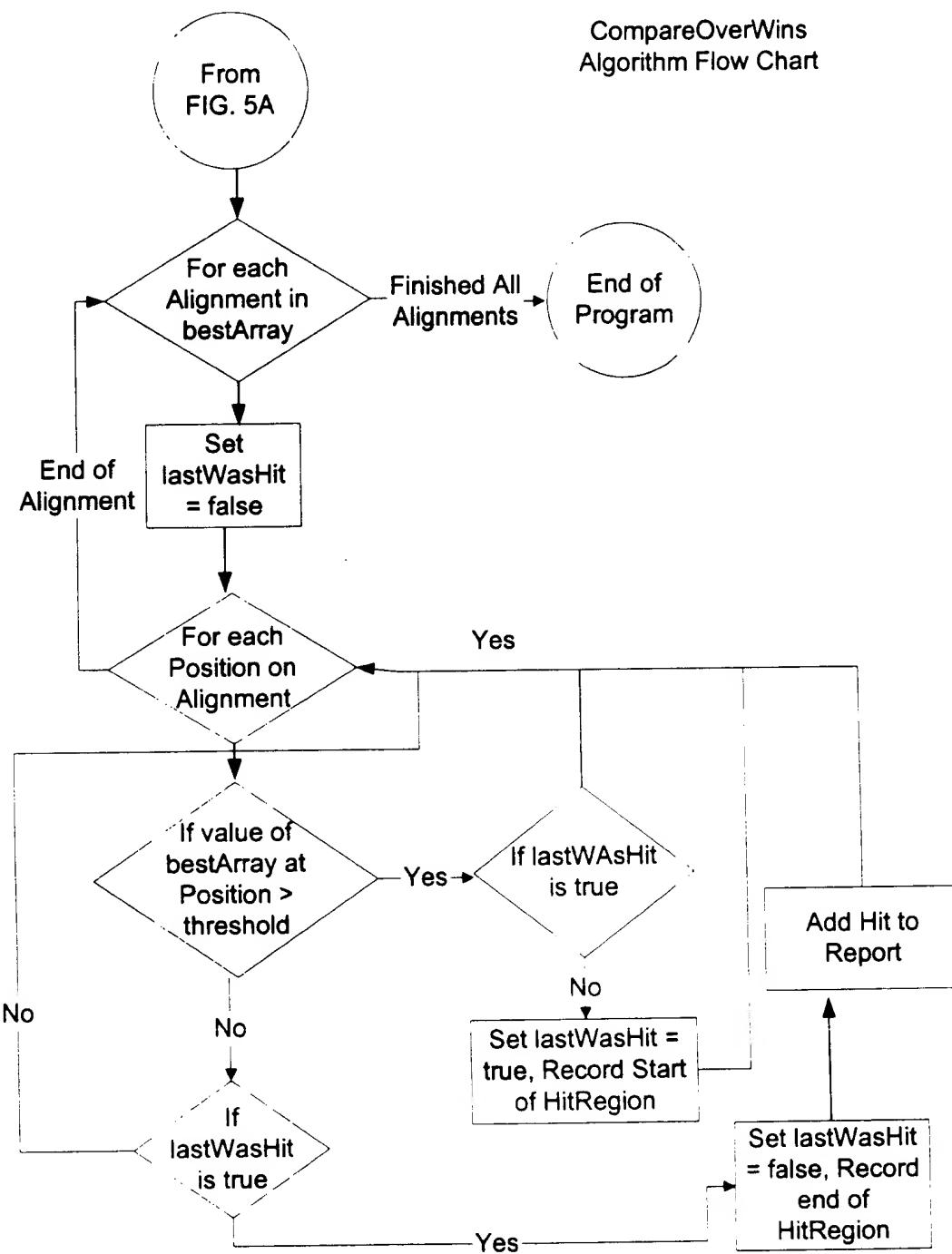


FIGURE 5B

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Input:
 Sequence A length a
 Sequence B length b
 Window Size

CompareOverWins
Algorithm Flow Chart
Basic Compare

Output:
 Array of size a by b of unsigned chars (0-255)
 Each point represents the number of matches in the
 window at that alignment and position

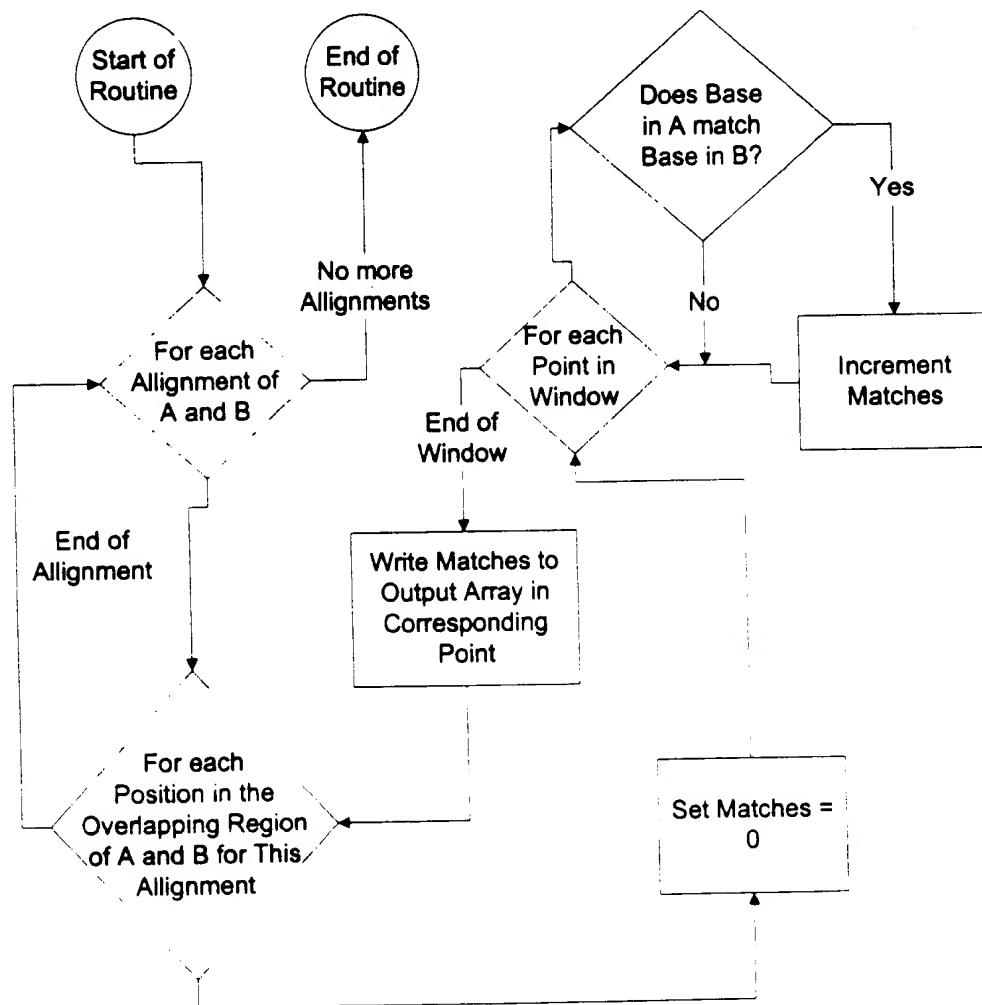
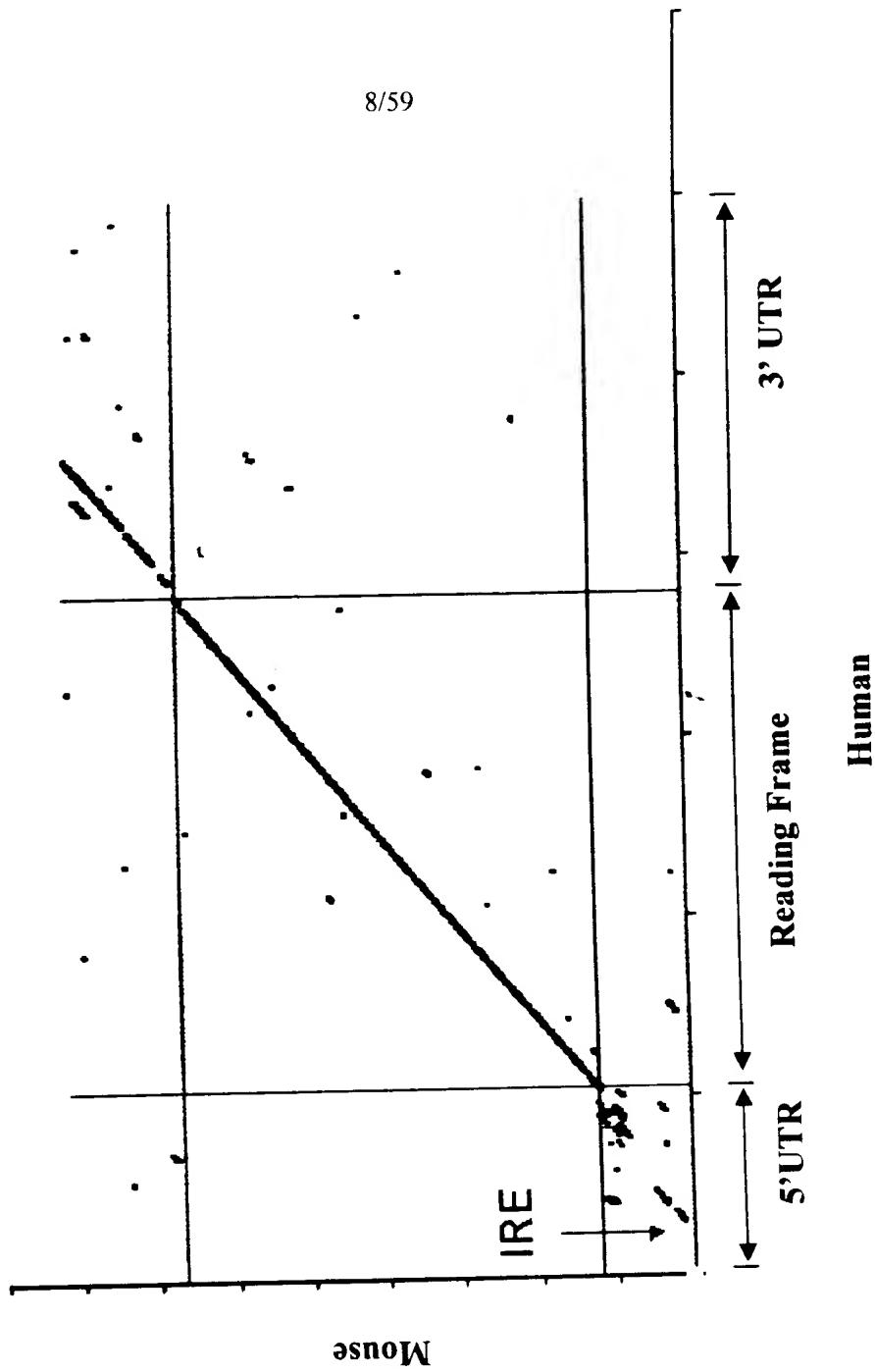


FIGURE 5C

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Figure 6



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Self Complementation Analysis - Single Sequence

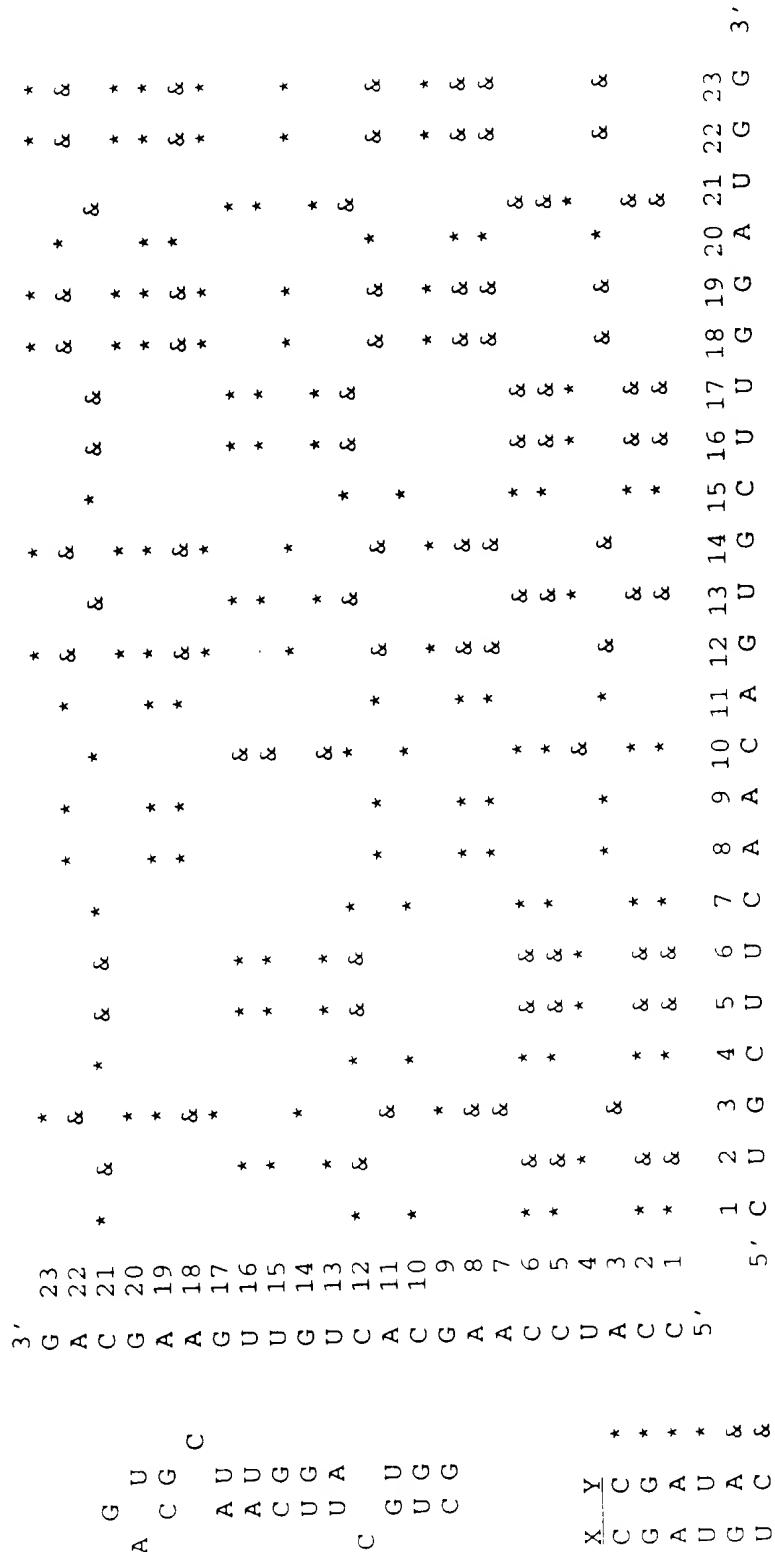


Figure 7

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Self Complementarity Comparisons

13 ortholog overlay

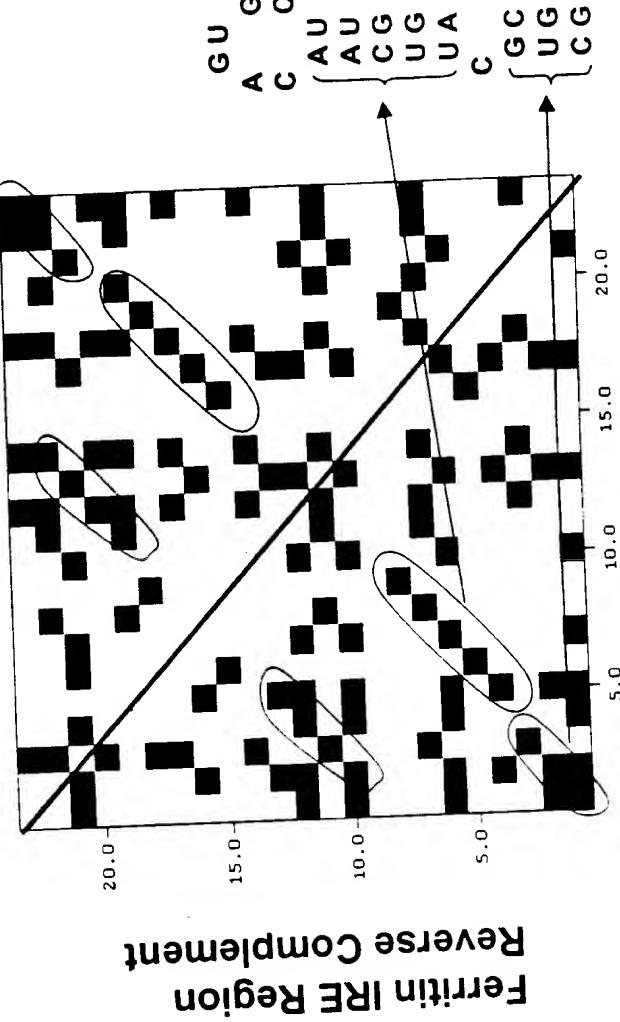
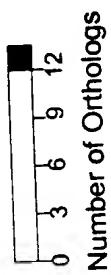


Figure 8

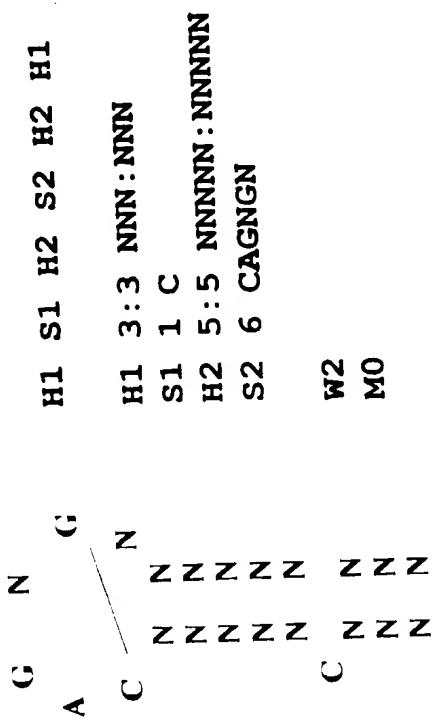


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IRE String descriptor

- This descriptor allows for
 - a wobble (W) of 2
 - no mismatches.
 - N can be any nucleotide
 - H refers to the stem region
- S refers to the single stranded region.

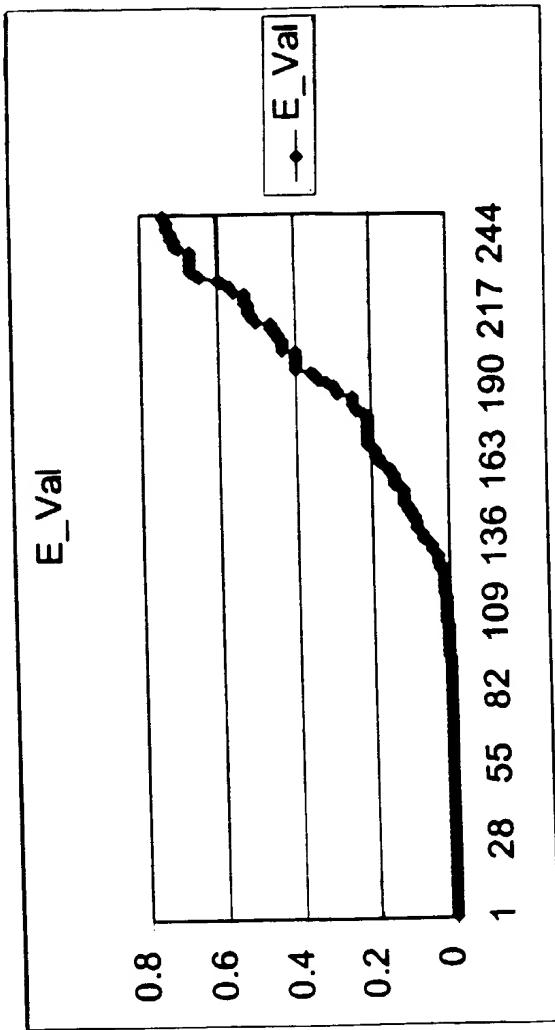
Figure 9



IIR-E Stem-loop Model

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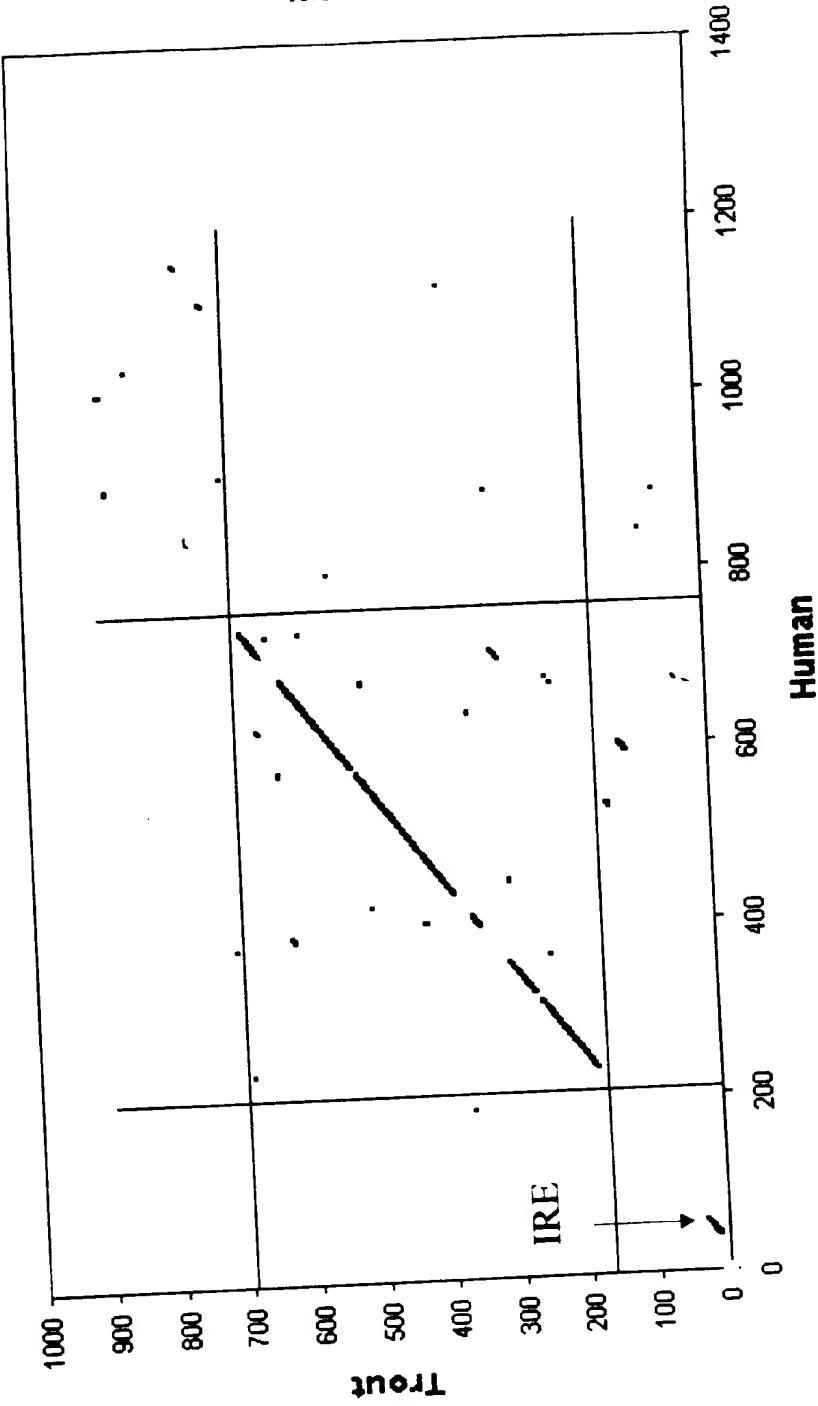
Figure 10



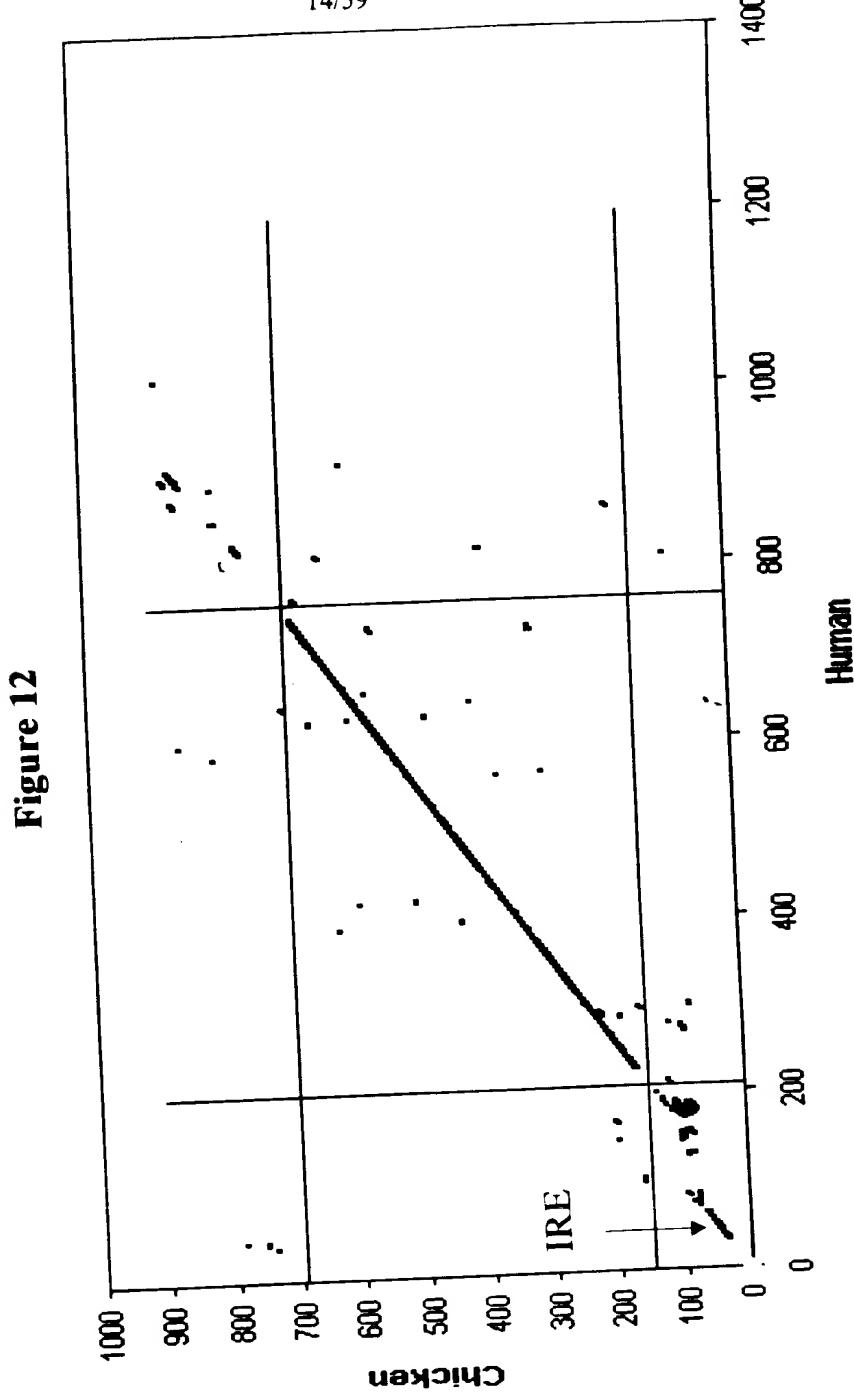
Document: IBIS-0007 Serial No. 09/076,404
Title: MODULATION OF MOLECULAR INTERACTION SITES ON RNA
AND OTHER BIOMOLECULES
Inventors: Dr. Michael J. K. Griffey, Stanley T. Crooke,
P. G. S. and E. S. C. Yedla, Venkatraman Mohan and Steve Hofstader
Attorneys: Paul K. Leggatt Attorney Phone No.: 215-564-8906
Sheet 13 of 59

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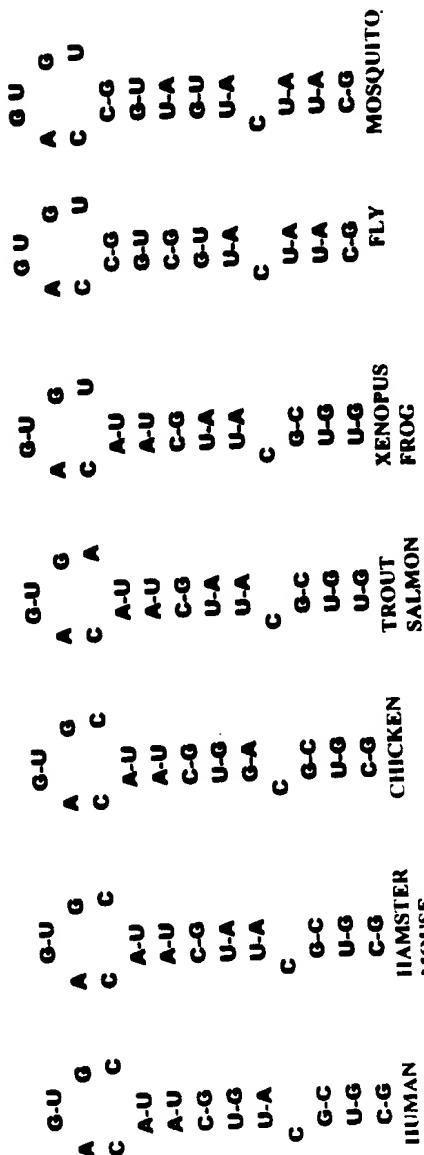
Figure 11



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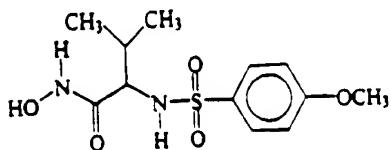


	No	No	Yes	Yes	Yes	No	No
HUMAN	No	No	Yes	Yes	Yes	No	No
PIG	No	No	Yes	Yes	Yes	No	No
HAMSTER			Yes	Yes	Yes	No	No
MOUSE		No	No	Yes	Yes	Yes	Yes
RAT			No	Yes	Yes	Yes	Yes
CHICKEN				No	Yes	Yes	Yes
TROUT					No	Yes	Yes
SALMON					No	Yes	Yes
XENOPUS					No	Yes	No
FROG					No	Yes	No
FLY					No	Yes	No
MOSQUITO					No	Yes	No

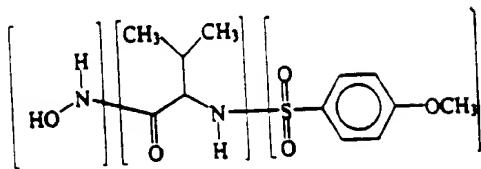
Figure 13

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Compound CI



C₁₂H₁₈N₂O₅S



Molecular formula F_i F_{ii} F_{iii}

H₂NO C₅H₉NO C₇H₇O₃S

Figure 14

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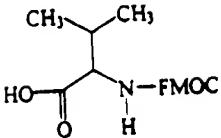
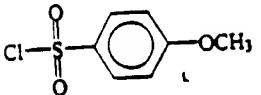
Addition of fragments to yield compounds

Table

Fragment Identifier	Structure	Name	Molecular formula	Other
F _i		Hydroxylamine	H ₂ NO	...
F _{ii}		Amino acid	C ₅ H ₉ NO	...
F _{iii}		Sulfonyl	C ₇ H ₇ O ₃ S	...

Figure 15

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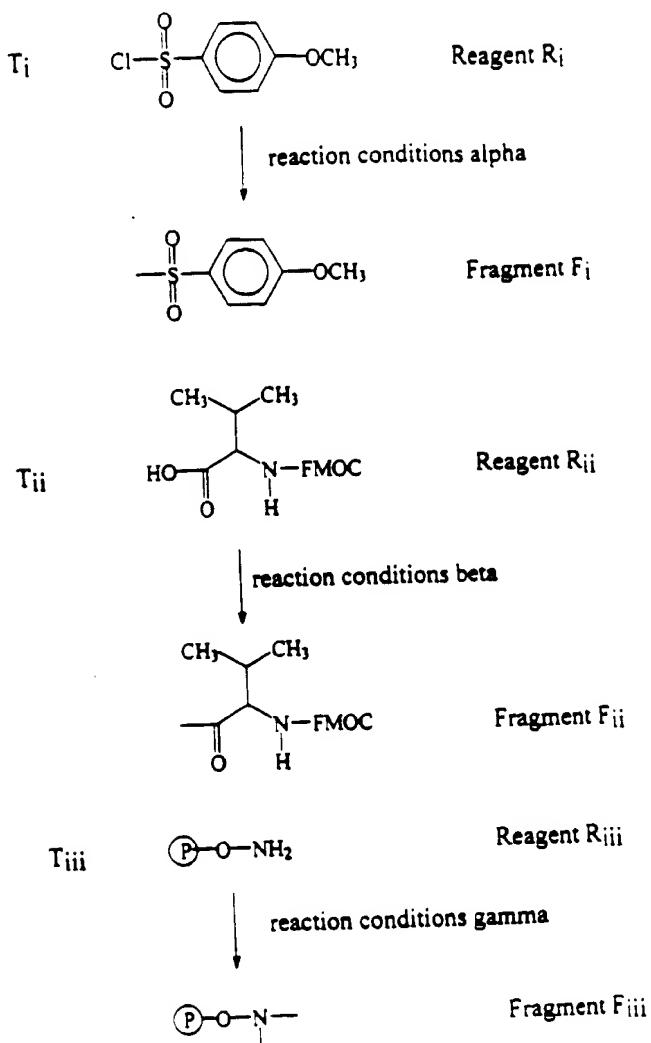
Reagents	Identifier	Name	Properties
$\text{H}-\text{O}-\text{NH}_2$ or $(\text{P})-\text{O}-\text{NH}_2$	R _i	Hydroxylamine	...
	R _{ii}	FMOC blocked amino acid	...
	R _{iii}	Sulfonylchloride	...

(P) = Solid support

Figure 16

19/59

Transformation



(P) = Solid support

Figure 17

20/59

Common Fragment / Different Reagents and Transformations

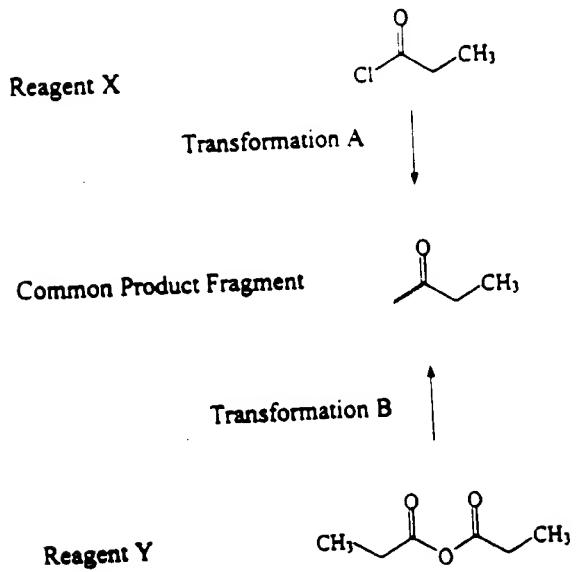


Figure 18

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Common Fragment / Different Reagents and Transformations

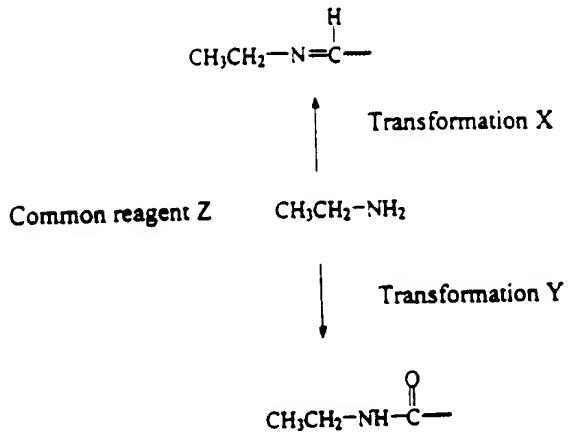


Figure 19A

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Common Reagent

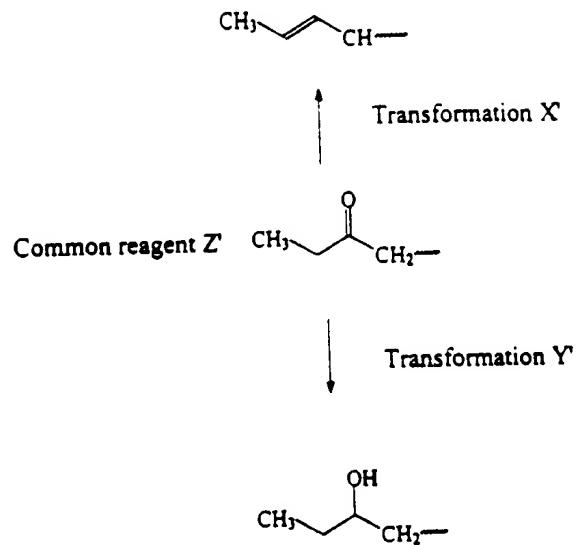


Figure 19B

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Symbolic addition of fragments to yield compound

Symbolic Structure Symbolic Identifier Molecular formula

Fragment



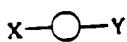
F_{i'}

C₀H_vN_w ...



F_{ii'}

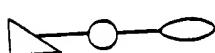
C₀H_vN_w ...



F_{iii'}

C₀H_vN_w ...

Compound



C_{i'}

C₀H_vN_w ...

Molecular formula F_{i'}

+

Molecular formula F_{ii'}

+

Molecular formula F_{iii'}

= Molecular formula C_{i'}

Figure 20

24/59

Symbolic Reagent Table

<u>Identifier</u>	<u>Name</u>	<u>Structure</u>	<u>Molecular formula</u>
R1	xxx		xxx
R2
R3
R4
R5
R6
R7
R8
R9
R10

Figure 21

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Symbolic Fragment Table

<u>Identifier</u>	<u>Symbolic Structure</u>	<u>Molecular formula</u>	<u>Molecular Weight</u>
F1		xxx	xxx
F2	
F3	
F4	
F5	
F6	
F7	
F8	

Figure 22

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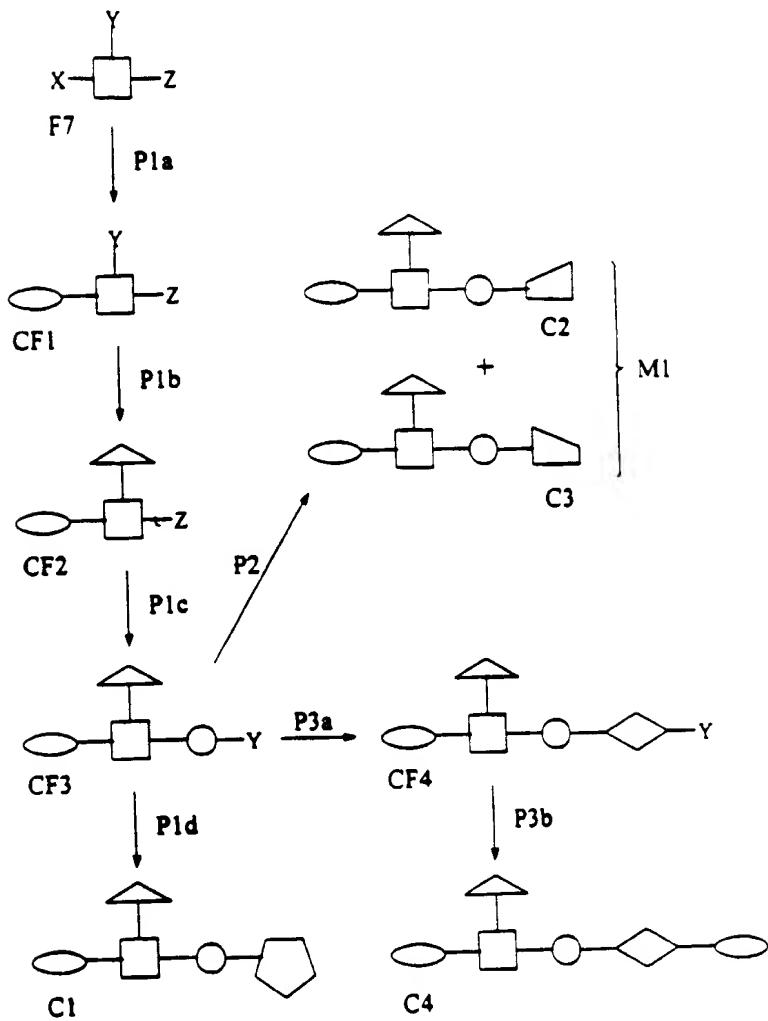
Symbolic Transformation Table

<u>Identifier</u>		<u>Symbolic Reactions</u>	<u>Reagent</u>
T1	F1	 ← R1	conditions α
T2	F2	 ← R2	conditions β
T3	F3	 ← R3	conditions α
T4	F3	 ← R4	conditions α
T5	F4	 ← R5	conditions α
T6	F5	X—  ← R6	conditions ϵ
T7	F5	X—  ← R7	conditions α
T8	F6	X—  ← R8	conditions α
T9	F7	X—  ← R9	conditions γ
T10	F8	X—  ← R10	conditions γ

Figure 23

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Single Compounds and Mixtures



P = synthetic path CF = complex fragment
F = fragment M = mixture
C = compound

Figure 24

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Mixture 2

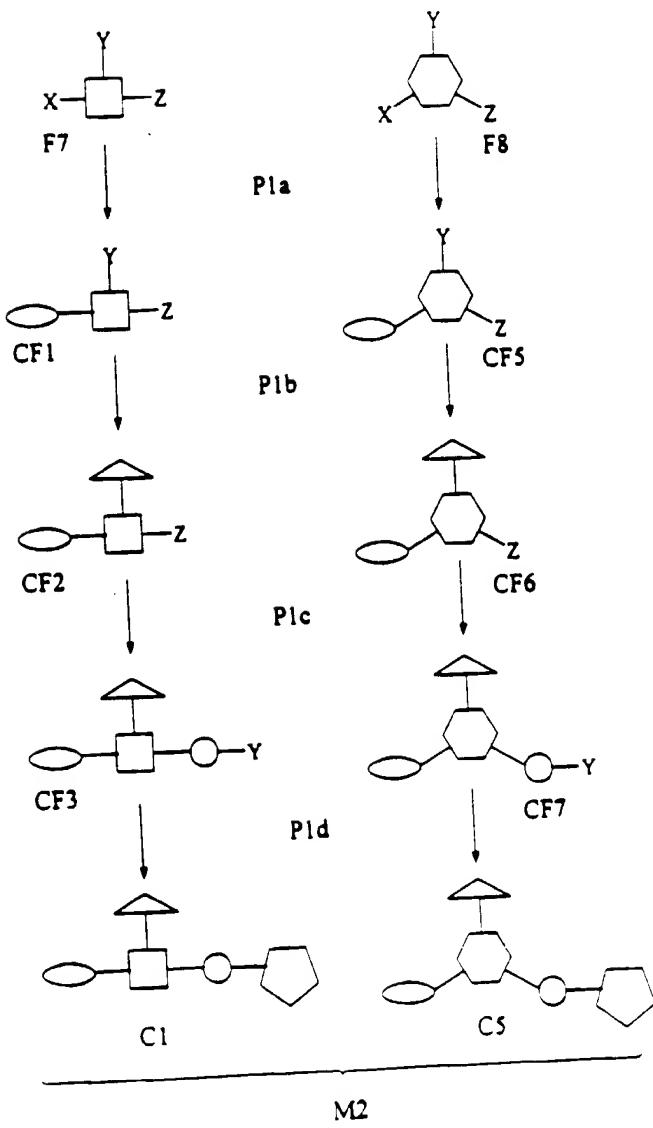


Figure 25

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Mixture 3

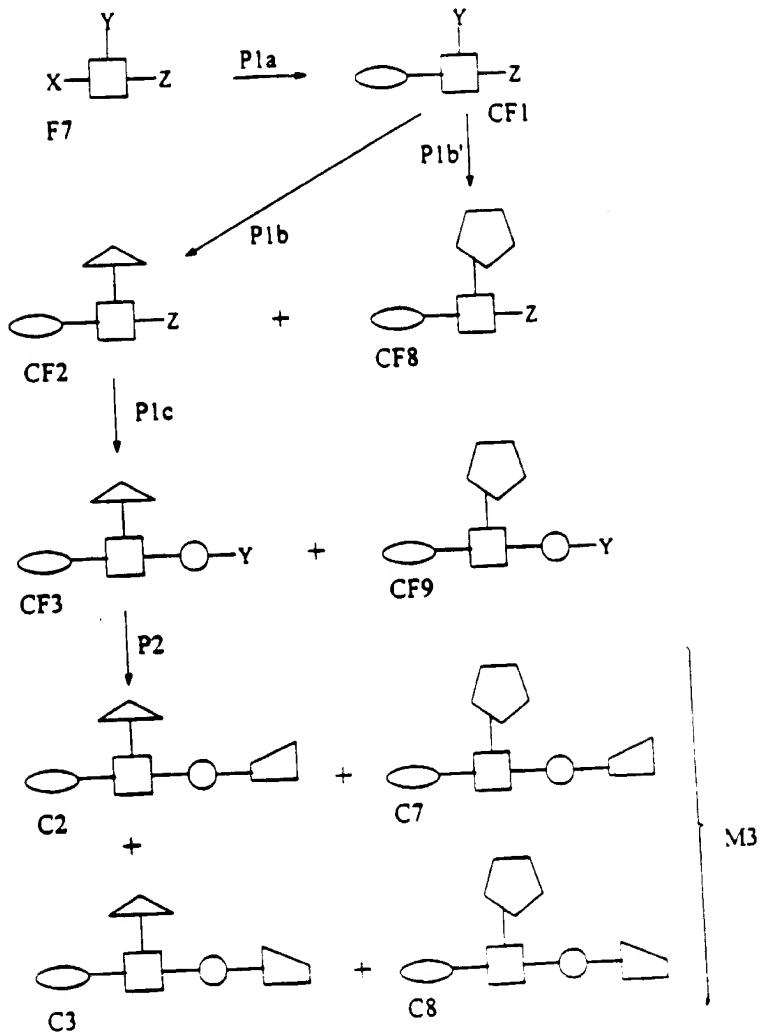


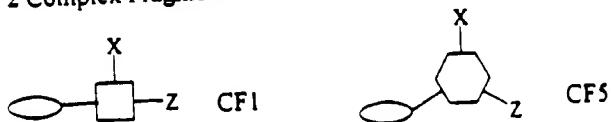
Figure 26

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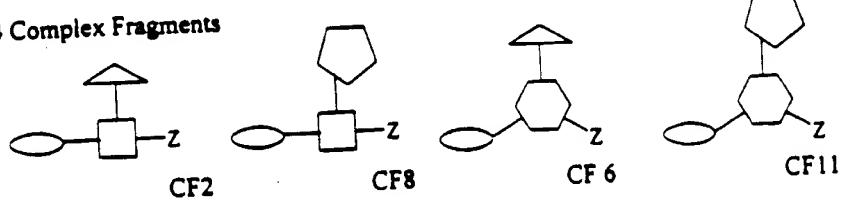
Mixture 4
2 Starting Fragments



2 Complex Fragments



4 Complex Fragments



8 Complex Fragments

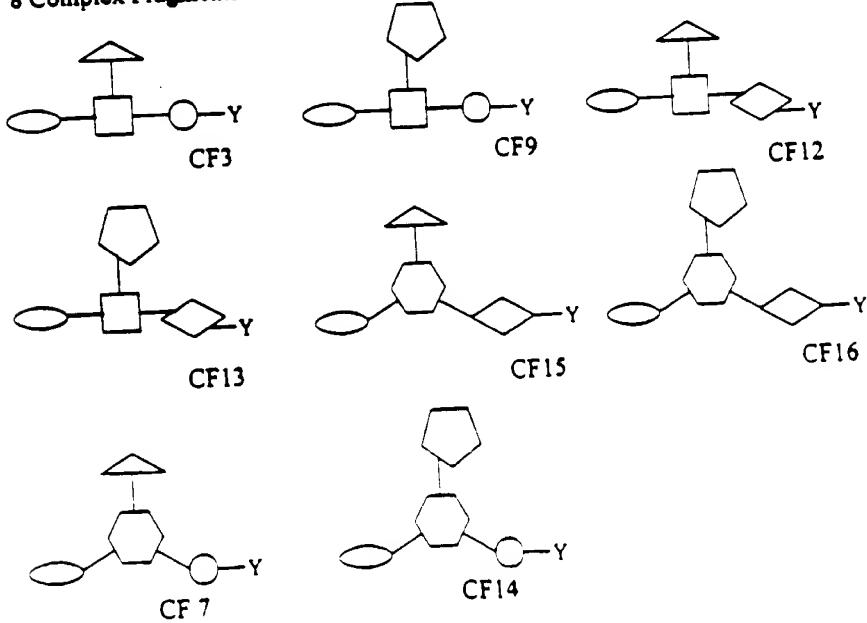


Figure 27A

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Mixture 4 (continued)

16 compounds

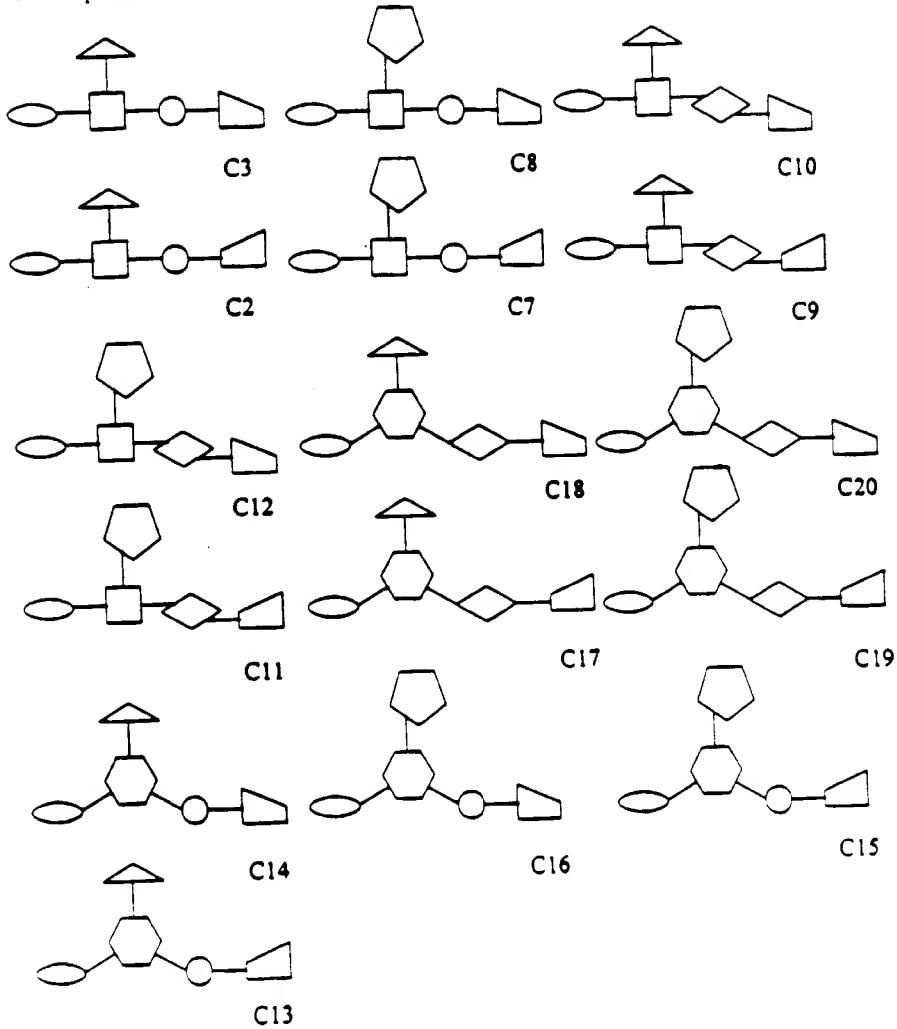


Figure 27B

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Tracking Table for Compound C1

(a) By Fragments:

n	n+1	n+2
F7		
	F2	
	F1	
	F5	
		F3

(b) By Transformations:

Synthesis Path 1

n	n+1	n+2
T9		
	T2	
	T1	
	T6	
		T3

Synthesis Path 2

n	n+1	n+2
T9		
	T2	
	T1	
	T7	
		T3

Synthesis Path 3

n	n+1	n+2
T9		
	T2	
	T1	
	T6	
		T4

Synthesis Path 4

n	n+1	n+2
T9		
	T2	
	T1	
	T7	
		T4

Figure 28

DocID: IBIS-0007 Serial No.: 091076404
Title: MODULATION OF MOLECULAR INTERACTION SITES ON RNA
AND OTHER BIOMOLECULES
Inventor: Dr. JAMES M. C. Griffey, Stanley T. Crooke,
Re: Plaintiff: James M. Griffey, Truman Mohan and Steve Hofstadler
Attorney: Paul K. Lippard Attorney Phone No.: 215-564-8906
Sheet 33 of 59

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Tracking Table

Tracking M1

Step 1	
T9	

Step 2	
T9	T2

Step 3	
T9	T2 T1

Step 4	
T9	T2 T1 T7

Step 5	
T9	T2 T1 T7 TS ¹

C2

Step 5	
T9	T2 T1 T7 TS ²

C3

Figure 29

Docket # IBIS-0007 Serial No.: 09/076 404
 Title: REGULATION OF MOLECULAR INTERACTION SITES ON RNA
 AND OTHER MOLECULES
 Inventor: Dr. M. Peter Giedd, Griffey, Stanley T. Crooke,
 Robert J. Lutz, Michael A. Abramson, Mohan and Steve Hofstader
 Attorney: Paul R. Legarda Attorney Phone No.: 215-564-8906
 Sheet 34 of 59

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Tracking Table

Tracking M2

Step 1		
n	n+1	n+2
T9		

Step 1		
n	n+1	n+2
T10		

Step 2		
n	n+1	n+2
T9	T2	

Step 2		
n	n+1	n+2
T10	T2	

Step 3		
n	n+1	n+2
T9	T2 T1	

Step 3		
n	n+1	n+2
T10	T2 T1	

Step 4		
n	n+1	n+2
T9	T2 T1 T7	

Step 4		
n	n+1	n+2
T10	T2 T1 T7	

Step 5		
n	n+1	n+2
T9	T2 T1 T7	T4

Step 5		
n	n+1	n+2
T10	T2 T1 T7	T4

C1

C5

Figure 30

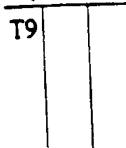
Docket No.: IBIS-0007 Serial No.: 09/076,404
Title: ISOLATION OF MOLECULAR INTERACTION SITES ON RNA
AND OTHER POLYNUCLEOTIDES
Inventor(s): David J. Leppla, John C. Griffey, Stanley T. Crooke,
Ranga Sampath, Eric C. Vining, Abraham Mohan and Steve Hofstadler
Attorney: Paul K. Legendre Attorney Phone No.: 215-564-8906
Sheet 35 of 59

35/59

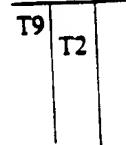
Tracking Table

Tracking M3

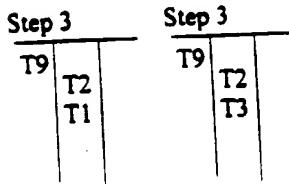
Step 1



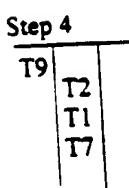
Step 2



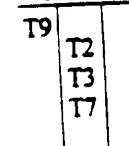
Step 3



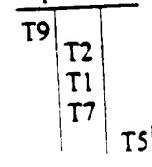
Step 3



Step 4

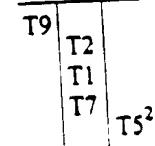


Step 5



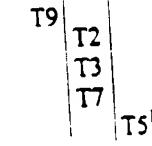
C2

Step 5



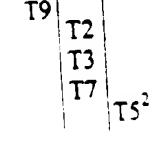
C3

Step 5



C7

Step 5



C8

Figure 31

Docket No. IBIS-0007 Serial No. 09/076,404
Title: REGULATION OF MOLECULAR INTERACTION SITES ON RNA
AND OTHER NUCLEIC ACIDS
Inventors: Paul J. Chirife, John C. Chirife, Stanley T. Crooke,
Rajendra Singh, V. Subramaniam Mohan and Steve Hofstadler
Attorneys: Paul J. Chirife, V. Subramaniam Mohan and Steve Hofstadler
Attorneys: Paul J. Chirife, Attorney Phone No.: 215-564-8906
Sheet 36 of 59

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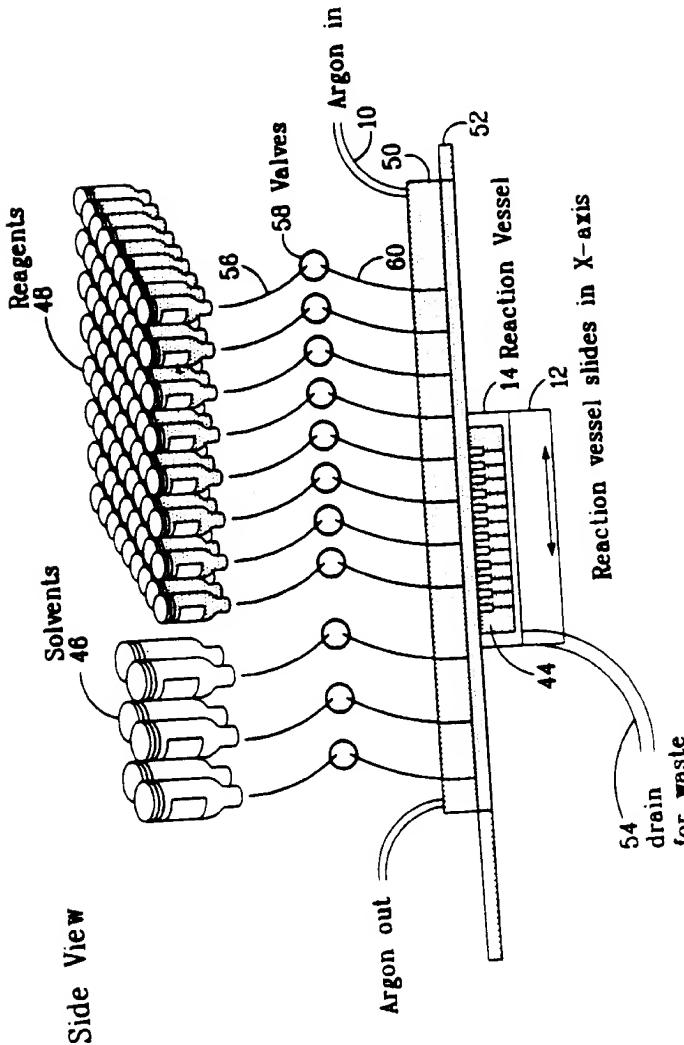


Figure 32

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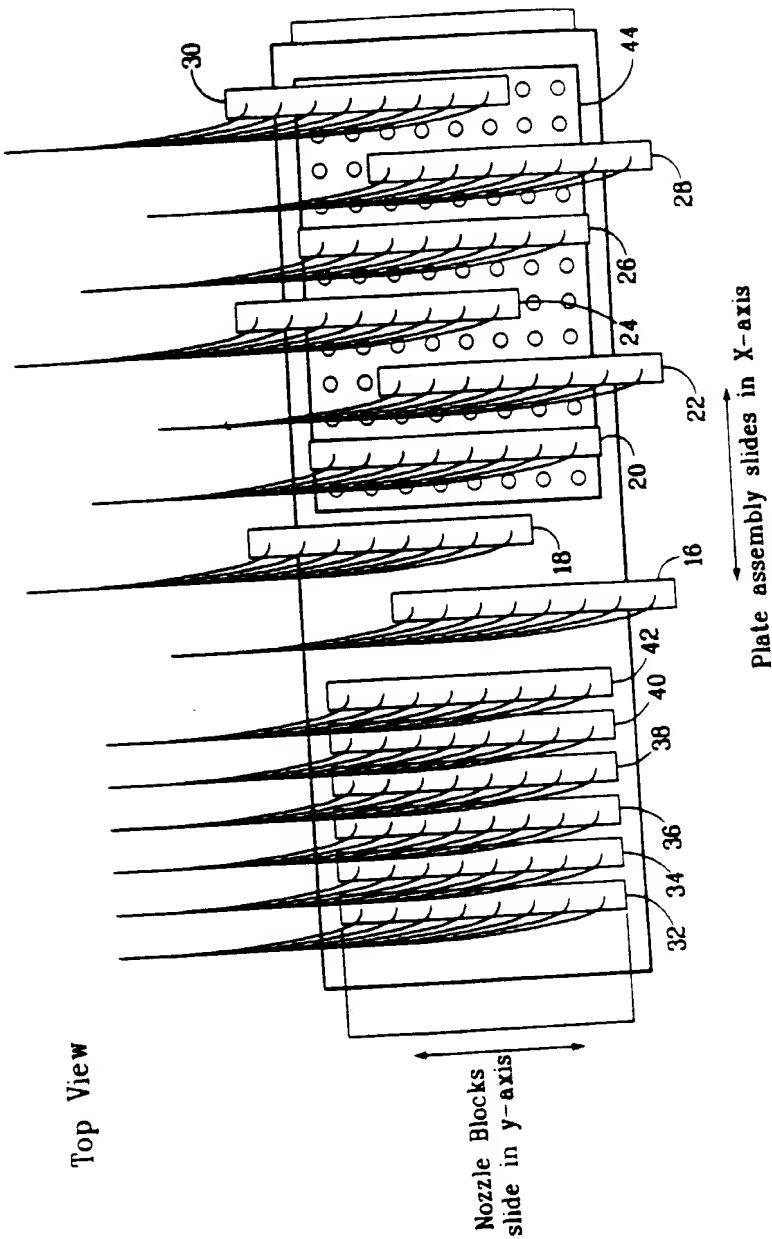


Figure 33

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Synthesis of hydroxamic acids from hydroxylamine resin

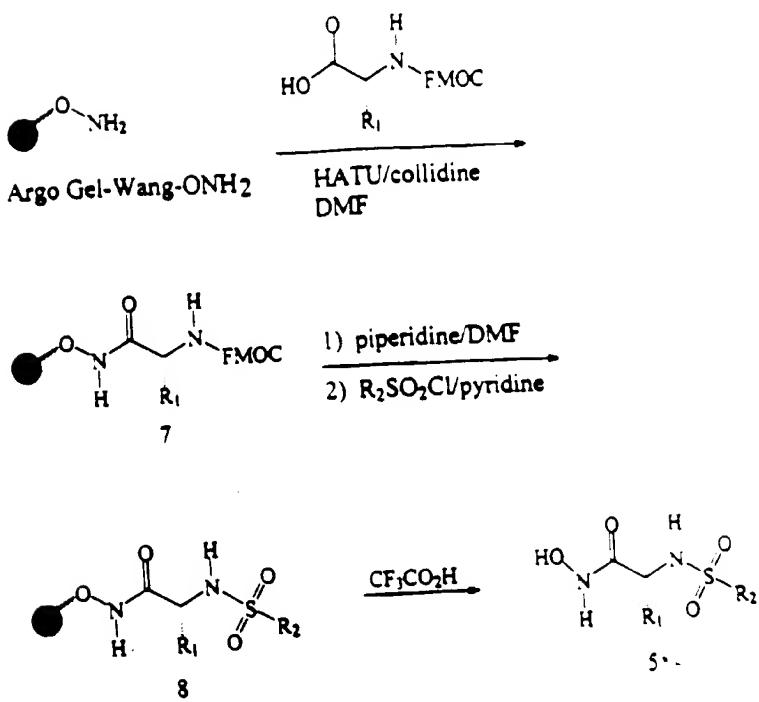


Figure 35

DocID: IBIS-0007 Serial No.: 09/078,404
Title: MODULATION OF MOLECULAR INTERACTION SITES ON RNA
AND OTHER BIOMOLECULES
Inventor(s): Daniel E. L. Fink, Richard Griffey, Stanley T. Crooke,
Randy G. Johnson, Michael J. Katze, Ramanathan Mohan and Steve Hofstadler
Purser, Inc., Philadelphia, PA Attorney Phone No.: 215-564-8906
Address: P.O. Box 1000, Philadelphia, PA 19101
Sheet 46 of 59

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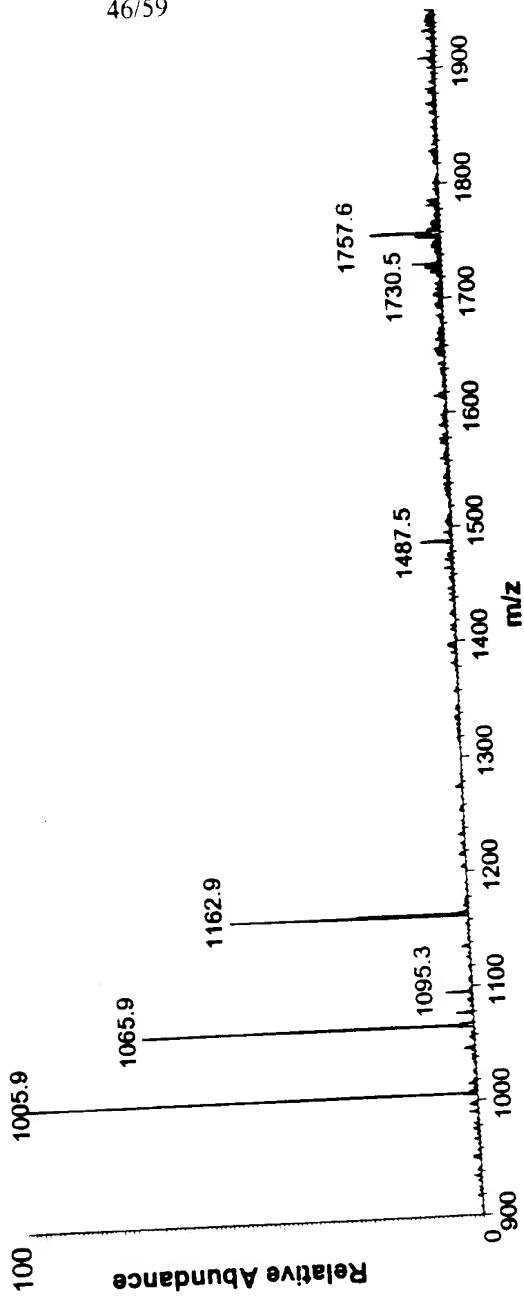


Figure 41A

DocID: IBIS-0007 Serial No.: 09/076,404
Title: MODULATION OF MOLECULAR INTERACTION SITES ON RNA
AND OTHER BIOMOLECULES
Inventor(s): [REDACTED] Griffey, Stanley T. Crooke,
Rajesh R. Katraman, Mohan and Steve Hofstader
Attorney: Paul K. Englund Attorney Phone No.: 215-564-8906
Sheet 47 of 59

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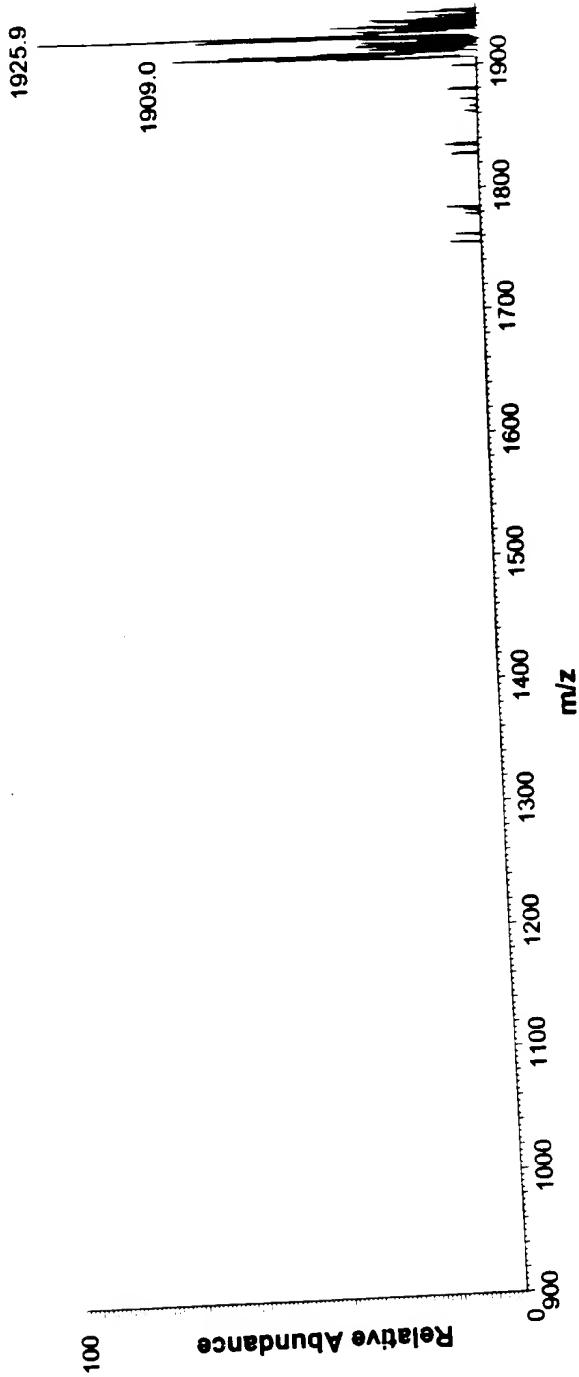


Figure 41B

Docket No. IBIS-0007 Serial No.: 09/076,404
Title: CALCULATION OF MOLECULAR INTERACTION SITES ON RNA
AND OTHER MOLECULES
Inventor: David E. Griffey, Stanley T. Crooke,
Randy C. Johnson, Alan L. Hartman, Mohan and Steve Hofstadler
Attorney: Pacific Legal, Inc. Attorney Phone No. 215-564-8906
Sheet 48 of 59

48/59

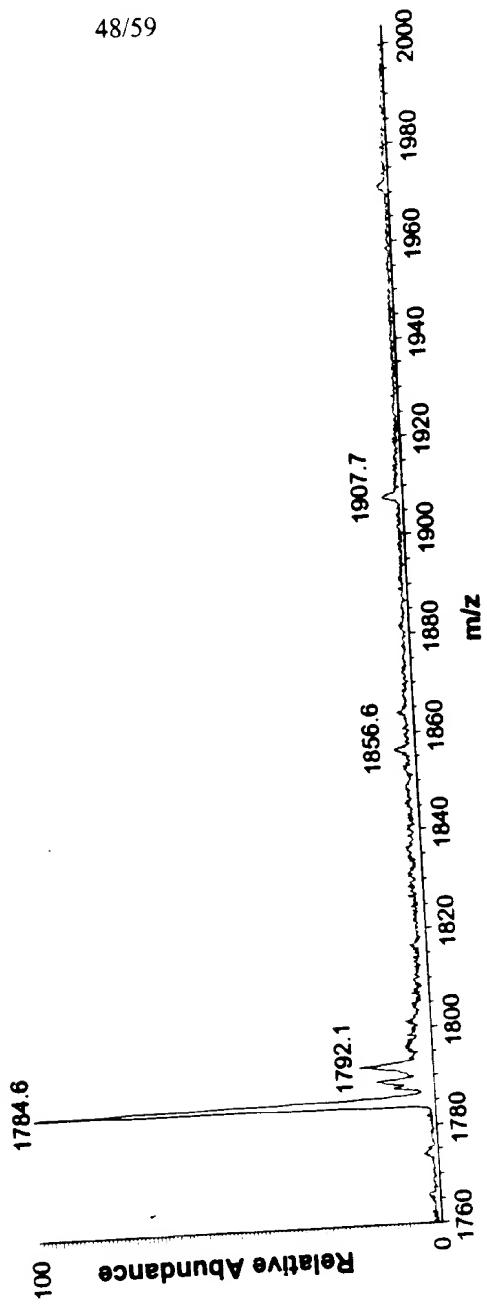


Figure 42A

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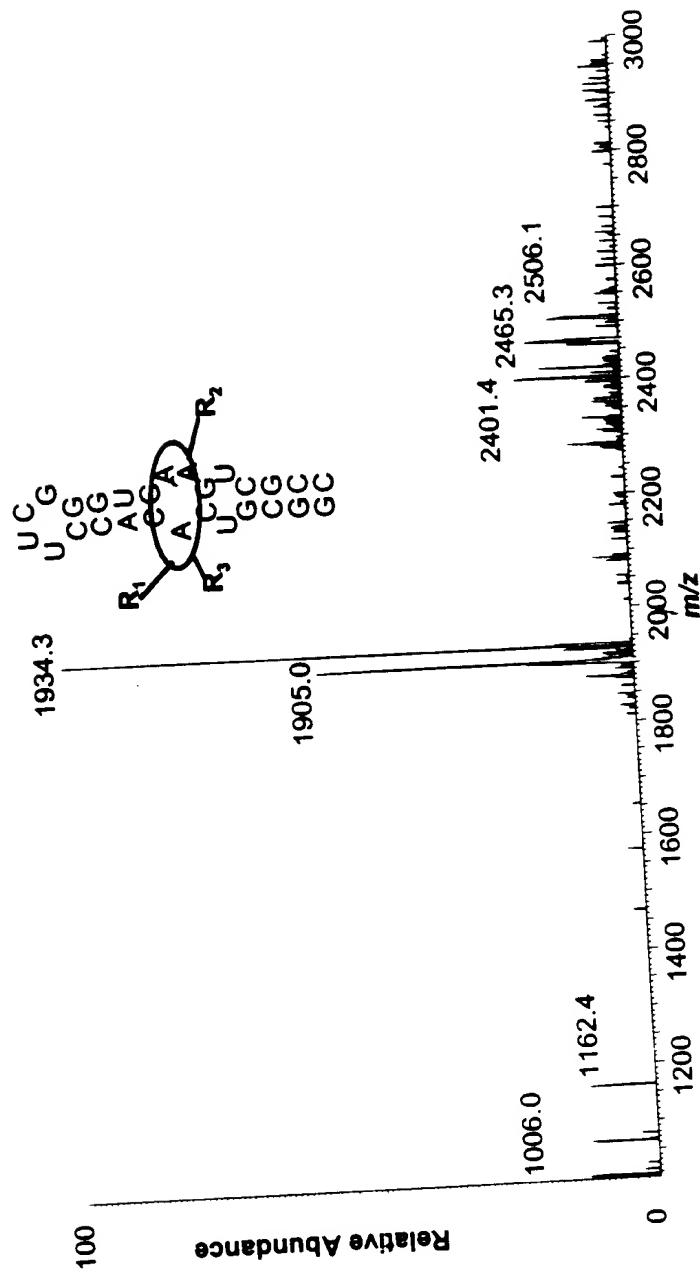


Figure 46

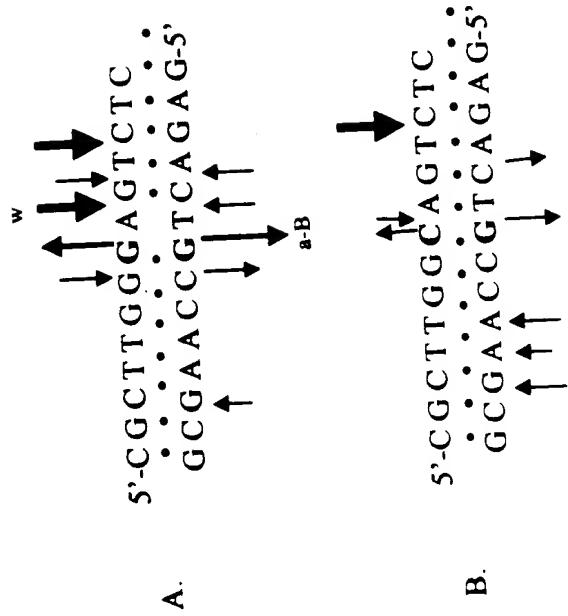


Figure 47

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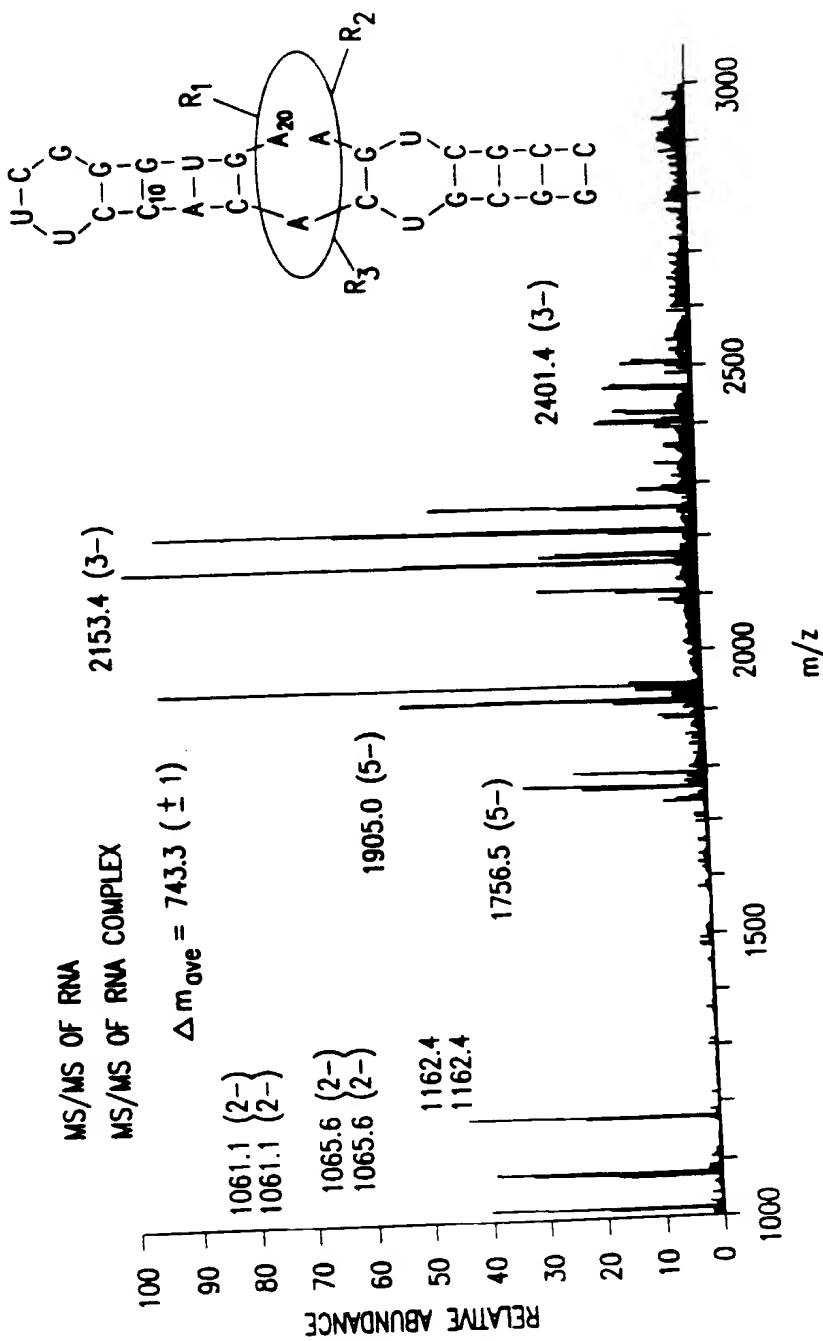


Figure 50

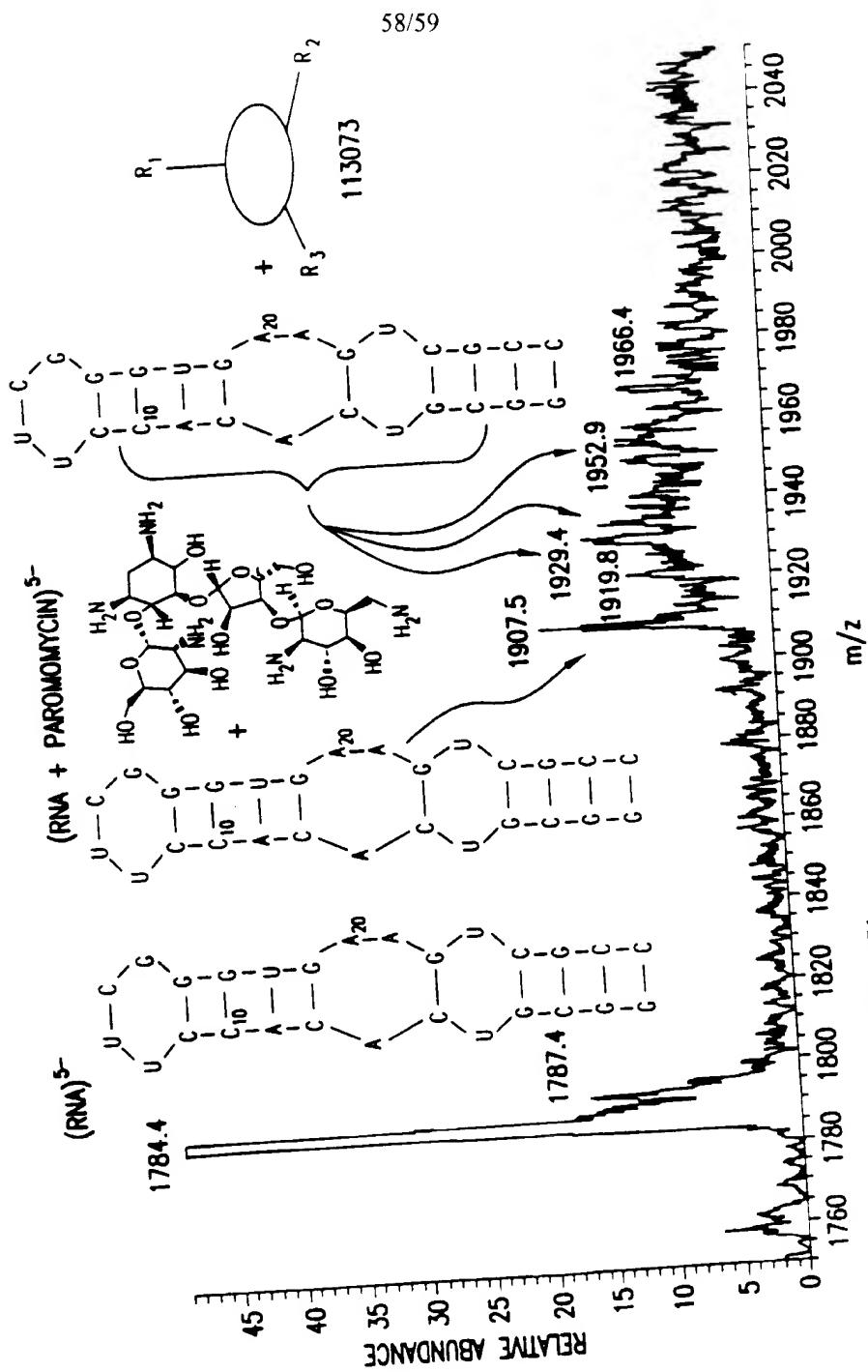


Figure 51

Doc. No.: IBIS-0007 Serial No.: 09/076,404
Title: MODULATION OF MOLECULAR INTERACTION SITES ON RNA
Against OTHER BIOMOLECULES
Attorneys: Paul K. Legaard, Richard Griffey, Stanley T. Crooke,
Ranga Sampath, Eric Swazze, Venkatraman Mohan and Steve Hofstadler
Attorney: Paul K. Legaard Attorney Phone No.: 215-564-8906
Sheet 59 of 59

59/59

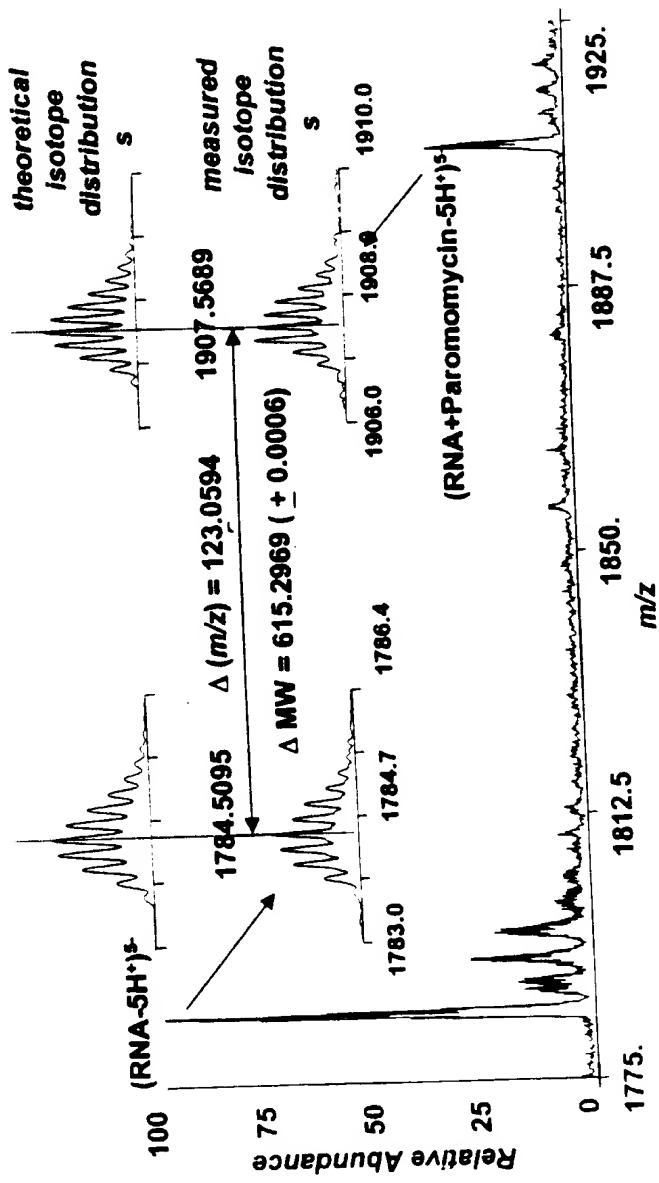


Figure 52